

In re Application of: Michal DANIELY et al
Serial No.:10/771,440
Filed: February 5, 2004
Office Action Mailing Date: March 20, 2008

Examiner: Duffy, Bradley
Group Art Unit: 1643
Attorney Docket: 26003

REMARKS

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 37, 39, 40, 54, 55, 57 and 72-81 are in this Application. Claims 37, 39, 40, 54, 55, 57 and 72-81 have been rejected under 35 U.S.C. § 112. Claims 37, 39, 40, 55, 57 and 72-81 have been rejected under 35 U.S.C. § 102. Claims 37 and 54 have been rejected under 35 U.S.C. § 103. Claims 37, 55, 72 and 73 have been amended herewith. Claims 74-81 have been canceled herewith.

In a telephone interview graciously granted by Examiner Bradley Duffy and Supervisor Stephen Rawlings on July 30th, 2008, the following issues were discussed.

With respect to the 102(b) rejections (Skacel et al.) and 103(a) rejections (Skacel et al. in view of US Patent No. 6,418,236), Applicants' representative stated that as shown in the color images of Figures 2A and 2B of Skacel et al., the cells which are stained with Papanicolaou (Figure 2A) and the cells which are stained with FISH (Figure 2B) represent different microscopic fields and thus the analyzed cells are necessarily different cells, which is thus in sharp contrast to the present teachings. Examiners indicated that amending the claims to recite "single cell" would tentatively overcome the outstanding rejections with respect to 102(b).

Examiners further indicated that other outstanding issues especially under 103 may arise after further consideration. In response, Applicants' representative noted the superior effect of analyzing at the single cell level especially to the field of cancer diagnosis. Examiner's attention was referred to the statistical results supporting the superiority which can be found in pages 29-34 of the instant specification as filed.

With respect to the 35 U.S.C. 112 rejections, the Examiners have provided claim language which may tentatively overcome the pending rejections. Applicants believe that current claim amendments are in line with the fruitful discussion.

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Objections to the Drawings

The Examiner has objected to the drawings because the specification discloses that Figures 1-4 are color drawings or photographs and a petition under 37 CFR 1.84(a)(2) has not been filed to accept color drawings or photographs in this case.

Attached is a petition under 37 CFR 1.84(a)(2) to accept the color drawings.

Specification

The Examiner has objected to the disclosure because of: (a) the use of improperly demarcated trademarks (e.g., UroVysion® on Page 17, line 11); (b) the specification does not include a paragraph indicating presence of color drawings ; and (c) minor errors in the specification;

Applicants have amended the specification as suggested by Examiner.

Amendments To The Claims

35 U.S.C. § 102 Rejections

Grounds of rejections maintained: The Examiner has maintained his rejections to claims 37, 39, 40, 55, 57 and 72-81 under 35 U.S.C. 102(b) as being anticipated by Skacel et al. (2001). Specifically, the Examiner states that Skacel et al. teach staining the same malignant transitional carcinoma cells with Papanicolaou stain and FISH probes specific to chromosomes 3, 7, 17 and 9p21 (Figure 2 legend) and accordingly, Skacel et al. teach processes that are materially and manipulatively indistinguishable from the claimed process and absent of a showing of any difference, the process disclosed by the prior art is deemed the same as the claimed process. Examiner's rejections are respectfully traversed. Claims 37, 55, 72 and 73 have now been amended.

Applicants point out that in contrast to Examiner's assertion Skacel et al. do not teach identifying transitional cell carcinoma or diagnosing bladder cancer by staining cells of a urine sample with Papanicolaou stain and FISH and identifying a

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morphological abnormality and a chromosomal abnormality in a single cell as now claimed.

Specifically, Applicants refer Examiner's attention to the color images of Figure 2A and 2B (bottom Page 383 in Skacel et al.) in which different microscopic fields and therefore different cells are shown. Thus, Figure 2A depicts an image of a microscopic field which includes 9 cells that are stained only with Papanicolaou stain (note the blue and purple shades in Figure 2A) and Figure 2B depicts another microscopic field which includes 2 cells that are stained with DAPI and FISH (note the red, green, aqua and gold signals resulting from FISH probes over the blue DAPI staining in Figure 2B). Thus, the color images of Figures 2A-B in Skacel et al. demonstrate, beyond any doubt, that Figures 2A and 2B are photographs of two different microscopic fields which necessarily include different cells. Accordingly, withdrawal of the rejections is respectfully requested.

Ample support for the amendments made in claims 37, 55, 72 and 73 can be found in the instant application as filed. See for example, Page 11: lines 5-6, "*morphological abnormality*"; lines 9-10, "*cells with abnormal morphology are identified*"; Page 11: lines 12-13 "*chromosomal abnormality*"; Page 11: lines 17-19, "*a cell is considered as a cancerous cell if it exhibits abnormal findings according to both staining methods*"; and Page 27 (from line 26) through Page 28 (line 7) (for example of identification of transitional cell carcinoma using morphological and chromosomal abnormalities); Pages 28 (lines 29-33) through 29 (lines 1-3) (for detection of both morphological and chromosomal abnormalities in a *single cell*) and Pages 1 (from line 33) through 2 (line 5), and Page 2 (from line 31) through Page 3 (line 20) (for examples of morphological or chromosomal abnormalities associated with transitional cell carcinoma).

In view of the above arguments and remarks Applicants believe to have overcome the 35 U.S.C. § 102(b), rejections.

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35 U.S.C. § 103 Rejections

Grounds of rejections maintained: The Examiner has maintained his rejections to claims 37 and 54 under 35 U.S.C. 103(a) as being unpatentable over Skacel et al., in view of US Patent No. 6,418,236. Specifically, the Examiner states that Skacel et al. teach staining the same cells with Papanicolaou stain and FISH probes, and that the deficiency of Skacel is that it does not expressly teach imaging the cells with an automated imaging device capable of dual imaging, however, US Patent 6,418,236 discloses that the microscope is capable of dual imaging to determine if the same cells are stained with two stains of interest. Thus, the Examiner states that it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to identify transitional cell carcinoma cells or diagnose bladder cancer from a urine sample, by staining nucleated cells of a urine sample by the methods of Skacel et al. and imaging the same stained cells with the automated microscope capable of dual imaging as taught by US Patent No. 6,418,236 to identify transitional cell carcinoma cells of diagnose bladder cancer. Examiner's rejections are respectfully traversed. Claims 37, 55, 72 and 73 have now been amended.

Applicants point out that since as described above, Skacel et al., describe staining of different cells with Papanicolaou and FISH and U.S. Patent No. 6,418,236 merely discloses a microscope capable of dual imaging it cannot be used to render the claimed invention obvious since none of them teach identifying a single cell exhibiting a morphological abnormality and a chromosomal abnormality as a transitional cell carcinoma as now claimed. Accordingly, the claimed invention is novel and inventive over the teachings of Skacel and US Patent No. 6,418,236, either alone or in combination.

In view of the above arguments and remarks Applicants believe that the art of Skacel et al. cannot be used to obviate the claimed invention when combined with US Patent No. 6,418,236.

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35 U.S.C. § 112 Rejections

New Grounds of Rejections

The Examiner has rejected claims 37, 39, 40, 54, 55, 57 and 72-81 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Specifically, the Examiner states that claims 37, 55, 72 and 73 recite staining cells by “May-Grunwald-Giemsa, Giemsa, Papanicolaou or Hematoxylin-Eosin” which are biological stains known to be used in multiple staining methods and are not staining methods per se, thus the claims merely provide the use of these stains, but since the claims do not set forth any steps involved in the staining process it is unclear what process applicant is intended to encompass, because it cannot be ascertained how those “stains” are to be used.

Applicants traverse Examiner's rejection. The claimed stains are well known to those of ordinary skill in the art of cell biology who will know especially in view of the instant specification how to implement same when effecting the claimed invention. Applicants have amended without prejudice claims 37, 55, 72 and 73 so as to add clarity. Applicants note this amendment is cosmetic and does not alter claim scope. Support for the amendments can be found on Page 5, lines 28-30 in the instant application as filed.

(b) The Examiner further states that claims 37, 39, 40, 54, 55, 57 and 72-81 are indefinite because claims 37, 55, 72 and 73 are directed to methods of identifying transitional cell carcinoma cells in a urine sample or diagnosing bladder cancer, yet the claims merely recite process steps to stain nucleated cells of the urine sample and image the stained cells. The Examiner states that there is no process step that clearly relates back to the purpose or objective of the claimed invention.

Applicants traverse Examiner's rejection. Applicants point that the amendments made in claims 37, 55, 72 and 73 in response to the 35 U.S.C. § 102(b) rejections overcome Examiner's present rejections (35 U.S.C. § 112 second

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paragraph). Support for the amendments is indicated above in response to the 102(b) rejections.

(c) The Examiner further states that claims 74-81 are indefinite for reciting "said FISH is effected using a FISH probe", and given that the term "effect" means "the result or consequence of an action" one of skill in the art would reasonably conclude that the claims merely provide the use of FISH probes without setting forth any steps involved in the process that would allow one of skill in the art to determine how these FISH probes are used to effect FISH.

Examiner's rejections are respectfully traversed, but in order to expedite prosecution of this case, Applicants have cancelled claims 74-81, thereby rendering moot Examiner's rejections.

The Examiner has rejected claims 37, 39, 40, 54, 57 and 72-81 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner states that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner states that claims 37, 39, 40, 54, 55, 57 and 72-81 are directed to methods of identifying transitional cell carcinoma cells in a urine sample and diagnosing bladder cancer by staining the nucleated cells by "May-Grunwald-Giemsa, Giemsa, Papanicolaou or Hematoxylin-Eosin" to thereby obtain stained nucleated cells and staining the stained nucleated cells by FISH and imaging the stained nucleated cells to thereby identify the transitional cell carcinoma or determine the presence or absence of cancerous cells within the stained nucleated cells; and that claims 74-81 further recite that said FISH is effected using a structurally and functionally diverse genus of "FISH probes to a pericentromeric region of chromosome 3, 7 and 17". The Examiner states that the claims (i) lack any active process step that sets forth how to identify transitional cell carcinoma or determine the presence or absence of cancerous cells; (ii) the claims are drawn to staining nucleated cells by "May-Grunwald-Giemsa, Giemsa, Papanicolaou

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or Hematoxylin-Eosin” terms which are commonly used to describe biological stains and not the staining methods *per se*; and (iii) the claims are directed to effecting FISH using a structurally and functionally diverse genus of “FISH probes to a pericentromeric region of chromosomes 3, 7 and 17” and it is submitted that the specification does not adequately describe the genus of FISH probes to which the claims are directed because there is no correlation of any particular identifying structural feature of these probes, however, the specification only adequately describes transitional cell carcinoma cells in urine samples with polyploidy for chromosomes 3, 7 and 17.

Examiner’s rejections are respectfully traversed.

Applicants believe that the amendments made in claims 37, 55, 72 and 73 in response to the U.S.C. 102(b) rejections overcome Examiner’s rejections. In addition, in view of cancellation of claims 74-81 Examiner’s rejections are rendered moot.

The Examiner has rejected claims 37, 39, 40, 54, 55, 57 and 72-81 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using methods encompassed by the claims, which are taught in the prior art, does not reasonably provide enablement for making and using the claimed methods. The Examiner states that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in the scope with these claims.

Examiner’s rejections are respectfully traversed.

Applicants believe that the amendments made in claims 37, 55, 72 and 73 in response to the U.S.C. 102(b) rejections overcome Examiner’s rejections.

In view of the claim amendments, arguments and remarks Applicants believe to have overcome the 35 U.S.C. § 112, rejections.

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Priority

The Examiner states that claims 37, 39, 40, 54, 55, 57 and 72-81 still do not properly benefit under §§ 119 and/or 120 by the earlier filing date of the priority document claimed, since the claims are rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description and/or a sufficiently enabling disclosure, and therefore the effective filing date of the claims is deemed the filing date of the instant application, namely February 5, 2004.

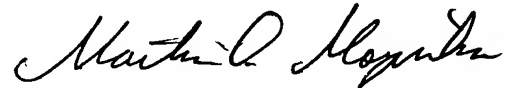
In view of the amendments above Applicants believe to have overcome the 35 U.S.C. § 112 first paragraph rejections and therefore respectfully request that the effective filing date of the claims would be the filing date of the U.S. Provisional Application, No. 60/459,992, April 4th, 2003.

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In view of the above amendments and remarks it is respectfully submitted that claims 37, 39, 40, 54, 55, 57, 72-73 are now in condition for allowance. A prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,



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Date: August 12, 2008

Enclosures:

Two-month extension fee; and
Petition for Color Drawings under 37 CFR 1.84(a)(2).